



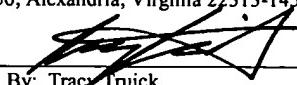
**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**Applicant:** Christian P. Larsen et al.      **Examiner:** Not yet known  
**Serial No.:** 10/057,288      **Group Art Unit:** 1646  
**Filed:** January 25, 2002      **Docket No.:** D0136NP/30436.58USU1  
**Title:** METHODS OF INDUCING ORGAN TRANSPLANT TOLERANCE AND CORRECTING HEMOGLOBINOPATHIES

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**CERTIFICATE UNDER 37 CFR §1.8:**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on June 13, 2003.

  
By: Tracy Truick

55 South Lake Avenue, Suite #710  
Pasadena, California 91101  
June 13, 2003

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**  
**(37 C.F.R. § 1.97(b)(3))**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Dear Sir:

This statement should be considered because it is submitted before the mailing date of the first Office Action on the merits according to 37 C.F.R. §1.97(b)(3). In accordance with 37 C.F.R. §1.98(d), copies of Exhibit 208-250 are provided herein.

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner. They are as follows:

- International Publication No. WO 01/90122 A2 published November 29, 2001 - **Exhibit 208**
- International Publication No. WO 01/54732 A1 published August 2, 2001 - **Exhibit 209**

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- International Publication No. WO 00/23115 published April 27, 2000 - **Exhibit 210**
- International Publication No. WO 97/28267 published August 7, 1997 - **Exhibit 211**
- International Publication No. WO 96/14865 published May 23, 1996 - **Exhibit 212**
- International Publication No. WO 95/34320 published December 21, 1995 - **Exhibit 213**
- International Publication No. WO 98/31820 published July 23, 1998 - **Exhibit 214**
- International Publication No. WO 94/28912 published December 22, 1994 - **Exhibit 215**
- U.S. Patent No. 6,444,792 issued September 3, 2002 - **Exhibit 216**
- International Publication No. WO 93/19767 published October 14, 1993 - **Exhibit 217**
- International Publication No. WO 94/29436 published December 22, 1994 - **Exhibit 218**
- International Publication No. WO 95/33823 published December 14, 1995 - **Exhibit 219**
- U.S. Patent No. 5,770,197 issued June 23, 1998 - **Exhibit 220**
- U.S. Patent No. 6,132,992 issued October 17, 2000 - **Exhibit 221**
- U.S. Patent No. 5,977,318 issued November 2, 1999 - **Exhibit 222**
- U.S. Patent No. 5,968,510 issued October 19, 1999 - **Exhibit 223**
- U.S. Patent No. 5,993,800 issued November 30, 1999 - **Exhibit 224**
- U.S. Patent No. 5,916,560 issued June 29, 1999 - **Exhibit 225**
- European Patent Publication Number 0 613 944 A2 published September 7, 1994  
**Exhibit 226**
- European Patent Publication Number 0 682 039 A1 published November 15, 1995  
**Exhibit 227**
- International Publication No. WO 93/00431 published January 7, 1993 - **Exhibit 228**
- International Publication No. WO 98/56417 published December 17, 1998 - **Exhibit 229**
- International Publication No. WO 95/34320 published December 21, 1995 - **Exhibit 230**
- International Publication No. WO 01/92337 published December 6, 2001 - **Exhibit 231**
- International Publication No. WO 98/33513 published August 6, 1998 - **Exhibit 232**
- U.S. Patent No. 5,958,403 issued September 28, 1999 - **Exhibit 233**

- Linsley, Peter S. et al., "Immunosuppression in Vivo by a Soluble Form of the CTLA-4 T Cell Activation Molecule," *Science*, 1992, 257:792-795 - **Exhibit 234**
- Morton, Phillip A. et al., "Differential Effects of CTLA-4 Substitutions on the Binding of Human CD80 (B7-1) and CD86 (B7-2)," *Journal of Immunology*, 1996, 156:1047-1054 - **Exhibit 235**
- Sun, Hong et al., "Prevention of Chronic Rejection in Mouse Aortic Allografts by Combined Treatment with CTLA4-Ig and Anti-CD40 Ligand Monoclonal Antibody," *Transplantation*, 1997, 64:1838-56 - **Exhibit 236**
- Souza, D. et al., "Synergistic Inhibition of Established Collagen Induced Arthritis (CIA) Through Dual Inhibition of ICAM-1 and CD40L Pathways," *Arthritis and Rheumatism*, 1999, 42:S60 - **Exhibit 237**
- Blazar, Bruce R. et al., "Coblockade of the LFA1:ICAM and CD28/CTLA4:B7 Pathways Is A Highly Effective Means of Preventing Acute Lethal Graft-Versus-Host Disease Induced by Fully Major Histocompatibility Complex-Disparate Donor Grafts," *Blood*, 1995, 85:2607-18 - **Exhibit 238**
- Alegre, Maria-Luisa et al., "Immunomodulation of Transplant Rejection Using Monoclonal Antibodies and Soluble Receptors," *Digestive Diseases and Sciences*, 1995, 40:58-64 - **Exhibit 239**
- Murakami, Masaaki et al., "Identification and characterization of an alternative cytotoxic T lymphocyte-associated protein 4 binding molecule on B cells," *Proceedings of the National Academy of Sciences USA*, 1995, 93:7838-7842 - **Exhibit 240**
- Peach, Robert J. et al., "Both Extracellular Immunoglobin-like Domains of CD80 Contain Residues Critical for Binding T Cell Surface Receptors CTLA-4 and CD28," *Journal of Biological Chemistry*, 1995, 270:21181-21187 - **Exhibit 241**
- Fargeas, Christine et al., "Identification of Residues in the V Domain of CD80 (B7-1) Implicated in Functional Interactions with CD28 and CTLA4," *Journal of Experimental Medicine*, 1995, 182:667-675 - **Exhibit 242**

- Steurer, Wolfgang et al., "Ex Vivo Coating of Islet Cell Allografts with Murin CTLA4/Fc Promotes Graft Tolerance," *Journal of Immunology*, 1995, 155:1165-1174 - **Exhibit 243**
- Guo, Yong et al., "Mutational Analysis and an Alternatively Spliced Product of B7 Defines Its CD28/CTLA4-binding Site on Immunoglobulin C-like Domain," *Journal of Experimental Medicine*, 1995, 181:1345-1355 - **Exhibit 244**
- Peach, Robert J. and Peter S. Linsley, "CTLA4Ig: A Novel Immunoglobulin Chimera with Immunosuppressive Properties," *Methods*, 1995, 8:116-123 - **Exhibit 245**
- Rattis, Frédérique-Marie et al., "Expression and function of B7-1 (CD80) and B7-2 (CD86) on human epidermal Langerhans cells," *European Journal of Immunology*, 1996, 26:449-453 - **Exhibit 246**
- Najafian, Nader and Mohamed H. Sayegh, "CTLA4-Ig: a novel immunosuppressive agent," *Exp. Opin. Invest. Drugs*, 2000, 9:2147-2157 - **Exhibit 247**
- Tan, Patrick et al., "Induction of Alloantigen-specific Hyporesponsiveness in Human T Lymphocytes by Blocking Interaction of CD28 with Its Natural Ligand B7/BB1," *Journal of Experimental Medicine*, 1993, 177:165-173 - **Exhibit 248**
- Turka, Laurence A. et al., "T-cell activation by the CD28 ligand B7 is required for cardiac allograft rejection *in vivo*," *Proceedings of the National Academy of Sciences USA*, 1992, 89:11102-11105 - **Exhibit 249**
- Scwhartz, R., "Costimulation of T Lymphocytes: The Role of CD28, CTLA-4, and B7/BB1 in Interleukin-2 Production and Immunotherapy," *Cell*, 1992, 71:1085-1088. **Exhibit 250**

No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art." Moreover, Applicants do not represent that the references have been thoroughly reviewed or that any relevance of any portion of a reference is intended.

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Filed: January 25, 2002  
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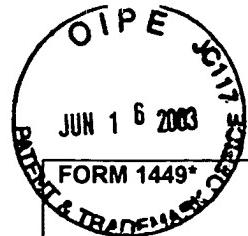
Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. § 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 50-0306.

Respectfully submitted,



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FORM 1449\*

**INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATION**

(Use several sheets if necessary)

Docket Number  
D0136NP/30436.58USU1Application Number  
10/057,288Applicant  
Christian P. Larsen et al.Filing Date  
January 25, 2002Group A Audit  
1644

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**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	6,444,792 (Exhibit 216)	09/03/02	Gray et al.			01/08/99
	5,770,197 (Exhibit 220)	06/23/98	Linsley et al.			01/22/93
	6,132,992 (Exhibit 221)	10/17/00	Ledbetter et al.			10/05/95
	5,977,318 (Exhibit 222)	11/02/99	Linsley et al.			06/07/95
	5,968,510 (Exhibit 223)	10/19/99	Linsley et al.			10/04/96
	5,993,800 (Exhibit 224)	11/30/99	Linsley et al.			06/06/95
	5,916,560 (Exhibit 225)	06/29/99	Larsen et al.			03/20/97
	5,958,403 (Exhibit 233)	09/28/99	Strom et al.			07/11/94

**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	WO 01/90122 A2 (Exhibit 208)	11/29/01	PCT				
	WO 01/54732 A1 (Exhibit 209)	08/02/01	PCT				
	WO 00/23115 (Exhibit 210)	04/27/00	PCT				
	WO 97/28267 (Exhibit 211)	08/07/97	PCT				
	WO 96/14865 (Exhibit 212)	05/23/96	PCT				
	WO 95/34320 (Exhibit 213)	12/21/95	PCT				
	WO 98/31820 (Exhibit 214)	07/23/98	PCT				
	WO 94/28912 (Exhibit 215)	12/22/94	PCT				
	WO 93/19767 (Exhibit 217)	10/14/93	PCT				
	WO 94/29436 (Exhibit 218)	12/22/94	PCT				
	WO 95/33823 (Exhibit 219)	12/14/95	PCT				
	EP 0 613 944 A2 (Exhibit 226)	09/07/94	EPO				
	EP 0 682 039 A1 (Exhibit 227)	11/15/95	EPO				
	WO 93/00431 (Exhibit 228)	01/07/93	PCT				

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.



FORM 1449* SUBSTITUTE DISCLOSURE STATEMENT IN AN APPLICATION  (Use several sheets if necessary)		Docket Number D0136NP/30436.58USU1	Application Number 10/057,288
		Applicant Christian P. Larsen et al.	
		Filing Date January 25, 2002	Group Art Unit 1644

**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	WO 98/56417 (Exhibit 229)	12/17/98	PCT				
	WO 95/34320 (Exhibit 230)	12/21/95	PCT				
	WO 01/92337 (Exhibit 231)	12/06/01	PCT				
	WO 98/33513 (Exhibit 232)	08/06/98	PCT				

**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

	Linsley, Peter S. et al., "Immunosuppression in Vivo by a Soluble Form of the CTLA-4 T Cell Activation Molecule," <i>Science</i> , 1992, 257:792-795 (Exhibit 234)
	Morton, Phillip A. et al., "Differential Effects of CTLA-4 Substitutions on the Binding of Human CD80 (B7-1) and CD86 (B7-2)," <i>Journal of Immunology</i> , 1996, 156:1047-1054 (Exhibit 235)
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	Souza, D. et al., "Synergistic Inhibition of Established Collagen Induced Arthritis (CIA) Through Dual Inhibition of ICAM-1 and CD40L Pathways," <i>Arthritis and Rheumatism</i> , 1999, 42:S60 (Exhibit 237)
	Blazar, Bruce R. et al., "Coblockade of the LFA1:ICAM and CD28/CTLA4:B7 Pathways Is A Highly Effective Means of Preventing Acute Lethal Graft-Versus-Host Disease Induced by Fully Major Histocompatibility Complex-Disparate Donor Grafts," <i>Blood</i> , 1995, 85:2607-18 (Exhibit 238)
	Alegre, Maria-Luisa et al., "Immunomodulation of Transplant Rejection Using Monoclonal Antibodies and Soluble Receptors," <i>Digestive Diseases and Sciences</i> , 1995, 40:58-64 (Exhibit 239)
	Murakami, Masaaki et al., "Identification and characterization of an alternative cytotoxic T lymphocyte-associated protein 4 binding molecule on B cells," <i>Proceedings of the National Academy of Sciences USA</i> , 1995, 93:7838-7842 (Exhibit 240)
	Peach, Robert J. et al., "Both Extracellular Immunoglobulin-like Domains of CD80 Contain Residues Critical for Binding T Cell Surface Receptors CTLA-4 and CD28," <i>Journal of Biological Chemistry</i> , 1995, 270:21181-21187 (Exhibit 241)
	Fargeas, Christine et al., "Identification of Residues in the V Domain of CD80 (B7-1) Implicated in Functional Interactions with CD28 and CTLA4," <i>Journal of Experimental Medicine</i> , 1995, 182:667-675 (Exhibit 242)
	Steurer, Wolfgang et al., "Ex Vivo Coating of Islet Cell Allografts with Murin CTLA4/Fc Promotes Graft Tolerance," <i>Journal of Immunology</i> , 1995, 155:1165-1174 (Exhibit 243)
	Guo, Yong et al., "Mutational Analysis and an Alternatively Spliced Product of B7 Defines Its CD28/CTLA4-binding Site on Immunoglobulin C-like Domain," <i>Journal of Experimental Medicine</i> , 1995, 181:1345-1355 (Exhibit 244)
	Peach, Robert J. and Peter S. Linsley, "CTLA4Ig: A Novel Immunoglobulin Chimera with Immunosuppressive Properties," <i>Methods</i> , 1995, 8:116-123 (Exhibit 245)

EXAMINER	DATE CONSIDERED
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\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE



<b>INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION</b>  (Use several sheets if necessary)	<b>Docket Number</b> <b>D0136NP/30436.58USU1</b>	<b>Application Number</b> <b>10/057,288</b>
	<b>Applicant</b>  Christian P. Larsen et al.	
	<b>Filing Date</b> <b>January 25, 2002</b>	<b>Group Art Unit</b> <b>1644</b>

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

**EXAMINER** \_\_\_\_\_ **DATE CONSIDERED** \_\_\_\_\_  
  
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\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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\*Substitute Disclosure Statement Form (PTO-1449)

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE